REMARKS/ARGUMENTS

In response to the final Office Action of May 2, 2007, Applicant has amended the claims, and cancelled claims 13 and 14, which when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

Claims 4, 5, 8, 13 and 14 remain rejected under 35 U.S.C.§ 112, first paragraph, as allegedly not supported by the written description. In order to advance prosecution of this application, Applicant has amended claim 4 to recite: "A method for the treatment of rheumatoid arthritis in a patient in need of such treatment comprising administering to the patient an effective amount of a CD25 binding molecule, wherein the CD25 binding molecule is basiliximab."

Support for claim 4 as amended may be found throughout the specification, e.g., page 5, lines 5-6, second half of page 7 through page 8, examples 1 and 2. Support for claim 8 as amended may also be found throughout the specification, e.g., page 6, final paragraph, to page 7, line 6. Applicant respectfully submits that claim 4 as presently amended, as well as claims 5 and 8 which depend therefrom, are fully supported by the written description of this application. Withdrawal of the rejection under the written description requirement of 35 U.S.C. 112, first paragraph, is therefore warranted.

Claims 4, 5, 8, 13 and 14 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over WO 89/09622 in view of Kovarik et al. (1997) *Transplantation 64*(12):1701-1705. WO '622 has been cited for teaching a method of treating rheumatoid arthritis (RA) comprising administering an effective amount of a CD25 binding molecule. The reference had also been cited for teaching the coadministration of a further substance effective in the treatment of RA, e.g., methotrexate.

Kovarik et al. has been cited for teaching a CD25 binding molecule comprising a CDR1, CDR2, and CDR3 having the amino acid sequences Arg-Tyr-Trp-Met-His, Ala-Ile-Tyr-Pro-Gly-Asn-Ser-Asp-Thr-Ser-Tyr-Asn-Gln-Lys-Phe-Glu-Gly, and Asp-Tyr-Gly-Tyr-Tyr-Phe-Asp-Phe, respectively (basiliximab). Kovarik et al. has also been cited for

teaching that serum concentrations of basiliximab sufficient to saturate IL-2 receptors were achievable.

Since the WO '622 reference teaches the use of a chimeric anti-IL2 receptor antibody for the treatment of RA, while Kovarik et al. teaches the chimeric anti-IL2 receptor antibody basiliximab which comprises the CDRs of the instant claims, the Examiner has concluded that the combined teachings of the two references amount to substitution of obvious equivalents. The Examiner has further posited that because the Kovarik et al. reference teaches that basiliximab can achieve IL2 receptor saturation and the antibody is well tolerated, basiliximab could be considered not only an equivalent of the antibody of the '622 patent but a preferred substitution of such antibody.

Applicants traverse the rejection under 35 U.S.C. §103(a) for the following reasons.

WO '622 refers exclusively to anti-Tac antibodies: the original mouse antibody and the humanized antibody obtained from it, i.e. comprising the variable regions from the mouse anti-Tac joined with constant region segments of human Immunoglobulin (see page 3, line 28-33). The variable regions of basiliximab presently recited in the claims is not the same as the variable sequences disclosed in WO '622.

Furthermore, WO '622 does not provide any data regarding the *in vivo* activity of the described antibodies, in particular regarding rheumatoid arthritis. This document does not provide any reasonable expectation of success of using antibodies directed to the IL-2 receptor for efficiently treating this specific disease. The fact that *in vitro*, a molecule has an activity on a receptor which is known to be involved in specific categories of diseases or disorders does not necessarily mean that this molecule will have an effect *in vivo*. In particular, Applicant respectfully submits that the fact that the IL-2 receptor may be a target for therapeutic approaches to T-cell mediated diseases, as taught on page 12 of WO '622, does not mean that any antibody which can interact with this receptor will be efficient *in vivo* for treating rheumatoid arthritis.

Because of the high complexity of the immune system in general and of the T-cell immune response in particular, the biological activity of such antibodies cannot be

explained and predicted only based on their capacity to bind to the targeted receptor. Other factors are very important to consider, including their physical properties (solubility, half-life in circulation, etc), their capacity of efficiently interacting with other components of the immune system, for example the complement, and their immunogenicity (which should be as minimal as possible). These factors are not directly predictable.

On page 5 of the office action, the Examiner has indicated that "Applicant appears to attempt to discredit the primary reference by arguing that it contains no *in vivo* data. Applicant's argument seems incredible given the fact that the instant specification itself discloses no *in vivo* data." The Examiner then directly quotes what the examiner believes is the entire teaching regarding the presently claimed invention.

In response, Applicant respectfully submits the following. Page 7, penultimate paragraph of the specification begins the *in vivo* study of the use of basiliximab in treating RA. 60 patients with active rheumatoid arthritis were studied. Page 8, lines 18-20, report the results of the study where patients receiving basiliximab show amelioration of symptoms as compared to patients receiving placebo.

That the work described therein is in the present tense, should not be interpreted to mean that the experiments were not actually conducted. MPEP § 608.01(p)(I) (Sept. 2007) provides that paper examples should not be represented as work actually done and that paper examples should not be described using the past tense. There is no prohibition however, in using present tense in describing work that has actually been done.

Koravik et al. describes the use of basiliximab in recipients of mismatched cadaver renal allografts. There is no indication or suggestion in this document that basiliximab would be suitable for treating rheumatoid arthritis. Further, the fact that serum concentrations of basiliximab can achieve IL2 receptor saturation is not enough to permit one skilled in the art to reasonably predict that basiliximab could be efficiently used for treating rheumatoid arthritis. Moreover, in the field of complex and not understood diseases such as rheumatoid arthritis, it is particularly difficult to make predictions about effective treatment and consequently there would not be any

reasonable expectations of success in treating rheumatoid arthritis using a CD25 binding molecule as presently claimed.

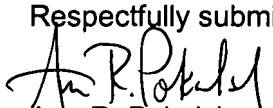
Applicant submits that it would have not been obvious for the skilled person to try using the CD25 binding molecules of the present application for therapeutic uses in rheumatoid arthritis with any reasonable expectation of success.

There is simply no teaching or suggestion in any of the references of record in this application that serum concentrations of basiliximab necessary to saturate the IL-2 receptor to suppress transplant rejections as taught by Kovarik et al. 1997, correlate to effectiveness in treating RA.

Applicant respectfully submits therefore, that one skilled in the art at the time the invention was made, having WO '622 and Kovarik (1997) in hand, as well as the literature extant (seven published examples of which were submitted on February 15, 2007, by supplemental response as full length papers), would not have found the presently claimed invention obvious.

In view of the foregoing remarks and amendments, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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